**Inflammatory bowel diseases**

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Abstract

**Objective:** to present a review about inflammatory bowel diseases in childhood so that pediatricians become familiar with two diseases (ulcerative colitis and Crohn's disease) that are increasing in incidence.

**Methods:** articles of specific gastroenterological journals were analyzed. Information was also obtained from the author's extensive professional experience in the area.

**Results:** the two diseases are described. Etiopathogenesis is obscure. Clinical presentation, diagnosis, and treatment are discussed, with details and practical aspects to enable the pediatrician to promptly understand the subject.

**Conclusions:** the inflammatory bowel disease is a condition of high morbidity, and the pediatrician who assists the case must have a very good technical knowledge about the disease, and must be very comprehensive and emotionally serene, in order to afford the young patient a better quality of life throughout the complicated evolution of this disease.


Introduction

Inflammatory bowel diseases are chronic, and its etiology is unknown. However, they may develop an immunologic inflammatory reaction in the digestive mucosa. They are represented by three diseases: nonspecific ulcerative colitis, Crohn’s disease, and undetermined colitis.

In cases of ulcerative colitis, only the colon is affected; in Crohn’s disease, any part of the digestive tract may be affected. Undetermined colitis happens when the colon is affected by an inflammatory process difficult to be characterized as nonspecific ulcerative colitis or Crohn’s disease.

These diseases are emerging and growing in the pediatric population, and the pediatrician should be alert, since at any moment he/she may face a child with one of these diseases, and should then be prepared to elaborate their diagnosis and to institute initial and sequential treatment.

**Nonspecific ulcerative colitis**

Nonspecific ulcerative colitis is an inflammatory disease that affects continuously the mucosa of the rectum and of the colon, and is clinically defined as a sanguineous diarrheal status.

**Epidemiology**

Until the 70s, nonspecific ulcerative colitis was very little reported in children, but its acknowledgment has been growing since then.

It is more common among white people, but in the author’s experience, 22% of the patients were mulattos. The incidence of the disease in the north of Europe and in the United States varies from four to eight cases per 100,000 people/year. In Brazil, there are no official data, but specialized services register a progressive increase in the number of patients that carry this disease.

It affects both genders in a similar proportion. Concerning age, it is usually more frequent in young adults between 20
and 40 years of age. In the pediatric group, the clinical status may be suggested from the 1st year of age on, but incidence peaks between 11 and 13 years of age. We stand out the great delay in the diagnosis, which may be of up to 4 years, thus intensifying the patients’ nutritional status. In the author’s experience, 22% of the patients presented the first symptoms at 2 years of age, 11%, at 3 years, and 67%, between 4 and 13 years of age.

Etiopathogenesis

Up to the present days, the etiology of nonspecific ulcerative colitis remains unknown, and although several factors are considered as possible etiologic agents, none was confirmed. The way how the inflammatory reaction is established, as well as its progression and perpetuation, are also investigated, but have not been clarified so far. Four factors continue to be investigated:

1) Infectious factor - its isolation as an agent responsible for the onset of colonic mucosa inflammation was not proved.
2) Psychogenic factor - some studies have been performed aiming at clarifying how a psychological aggressor can cause serious histological lesions in the colon.
3) Environmental factor (diet, smoking) - this was not confirmed either.
4) Genetic factor - familial studies are consistent with polygenic inheritance. The genetic markers studied show an increase in the frequency of HLA-D27 antigens between the carriers of nonspecific ulcerative colitis and ankylosing spondilitis. In Japan, the most frequent antigen associated with nonspecific ulcerative colitis is HLA-B5-DR2.
5) Immunologic factor - the participation of the immunologic system in the etiogenesis of nonspecific ulcerative colitis is accepted by most authors, and although there are many works about the subject, the basic mechanism involved is not defined yet. Humoral and cellular immunologic elements have not proven to participate in the inflammatory reaction of the disease. Some examples are the increase in the immunocytes that form IgG1 and IgG3, mast cells, macrophages, and others, but the importance of each of these elements in the reaction has not been established yet.

Pathological anatomy

The lesion affects the whole colon, starting at the rectum and propagating continuously to the entire colon, not overpassing the ileo-cecal valve. It affects only the mucosa, not all the colonic wall - there are some exceptions, though (in case of toxic megacolon, for example).

The active lesion is represented as mucosal congestion and edema, fociuses of epithelial necrosis, cryptic abscesses, and ulcers. The neutrophilic and lymphoplasmocytic infiltrate is outstanding. With favorable therapeutic response, the inflammatory process is reduced, with the disappearance of ulcers, reepithelization, and hyperplasia of crypts, leading to the formation of pseudopolyps. When clinical remission occurs, these crypts may suffer atrophy, with the thinning of mucosa, and shortening of crypt distortion, whose fundi were distal form the mucosal muscular.

Studies about the identification of HLA-DR expression in the colonic epithelial cells, using immunohistochemical methods, showed the inappropriate presence of this expression in cells of the colonic mucosa of patients presenting nonspecific ulcerative colitis. Rodrigues also showed this expression in patients with nonspecific ulcerative colitis and Crohn’s disease. In one patient, whose initial diagnosis was allergic colitis at 10 months of age, the mucosa already presented this expression. This author proposes the use of this technique to distinguish, in the young infant, the allergic colitis from the nonspecific ulcerative colitis, since in cases that prove to have allergic origin, this expression is absent, as happens in normal individuals.

Pathophysiology

Due to the compromising of the colonic and rectal mucosa, diarrhea presents with mucus, blood, and sometimes pus. The alteration of the motility, with the disappearance of haustrations, reduction of colonic caliber and length due to the inflammatory process, intensify the diarrhea and cause colic and tenesmus. Because of the ulcers, there is loss of proteins, and because of loss of useful colonic area, there is reduction of water and sodium absorption.

Clinical status

Nonspecific ulcerative colitis is a cyclic disease, with exacerbation and remission phases, and with a very variable degree of intensity.

The onset of symptoms may be either insidious with a posterior aggravation, or abrupt and serious. The symptoms are abdominal pain, diarrhea with or without blood, tenesmus, and urgency to defecate. The presence of nocturnal defecation is very characteristic.

Other data are anorexia, loss of weight, nausea, vomiting, jaundice, oral aphthae, and angular chelitis. If the diarrhea is too intense, it may be accompanied by dehydration and angular electrolytic disequilibrium, with hyponatremia and hypokalemia; the latter is a sign of development of toxic megacolon.

Although nonspecific ulcerative colitis is defined as a colonic disease, it presents in its clinical presentation several extradigestive symptoms (such as arthritis of the hip and knee), which may precede the appearance of digestive symptoms. Ocular problems, such as conjunctivitis and uveitis, may appear later. Gangrenous pyoderma and erythema nodosum may occur in 1% of the cases in the initial or late phases of the disease.
The disease may have a fulminant evolution, with a toxic status, massive hemorrhage, toxic megacolon, perforation, and death. In the author’s experience, this pattern occurred in 10% of the cases.\(^1\)

The disease may evolve to total cure after the first episode. However, this situation, besides being exceptional, is discussable, since in pediatrics, especially in young infants, these aspects may be mixed up with allergic colitis (whose histological and endoscopic aspects may be similar), and allergic colitis is transitory, with total cure.\(^1\)

Another evolutive form of the disease is the recurrent or recidivous intermittent chronic ulcerative colitis. This is the most frequent form, and is characterized by an acute crisis, followed by a phase almost completely asymptomatic, without symptoms or with moderate symptoms of pain, smooth feces, and eventual extradigestive symptoms.

The fourth form of nonspecific ulcerative colitis is the chronic continuous one, with a frequency of 10%. Its treatment is very complicated: frequent changes in the drug scheme, and vigilance aiming at the prevention or detection of complications are necessary. The patient’s general status deteriorates with the evolution of the disease, and growth deficit and pubertal delay occur, requiring surgical treatment.

The extension of the diseases varies a lot, but the rectum is always affected; the involvement of sigmoid and colon present variable frequencies. The ileum may be affected by insufficiency of the ileocecal valve and appearance of reflux ileitis.

The disease is evolutive, so a case in which initially only the rectum is affected may extend to the whole colon as time goes by.

Of the complications, the most serious one is the toxic megacolon, with an intense compromising of the colon, which dilates and thus causes intense pain, vomiting, absence of hydroaerial sounds, and general toxicity. A rigorous intensive treatment is necessary, with absolute fasting and total parenteral feeding; toxic megacolon must be considered a surgical emergency.\(^1\)\(^,\)\(^1\)\(^1\)

Another acute and serious complication is massive hemorrhage, which should be treated with the reposition of blood and hydrocortisone intravenously. This should also be considered an emergency surgical situation.

The most feared long-term complication is malignity, with the appearance of colonic cancer. So, every 10 years, colonoscopy and serial biopsies have to be performed for the early detection of the colonic cancer.\(^1\)\(^3\)

Nonspecific ulcerative colitis may be associated with liver diseases, such as sclerosing cholangitis, chronic active hepatitis, and hepatic steatosis, in 5% of the cases.\(^1\)\(^4\) Physical examination of the patient presenting nonspecific ulcerative colitis should include nutritional assessment, dermatological alterations, abdominal inspection and palpation, and examination of the anus.

Depending on the intensity and duration of the process, the nutritional status may be compromised or not. Examination of the mouth should always be performed in search for aphthae. The abdomen should be inspected, palpated, percussed, and auscultated for the assessment of abdominal distension, tympanitis, hydroaerial sounds, location of painful segments, or presence of hepatomegaly. There is no possibility of palpating abdominal mass in the patient with nonspecific ulcerative colitis; only the sigmoid and the colon can be palpated, as painful hard rolls. Perineal examination is mandatory, with rectal inspection and touch; the presence of lesions may suggest the diagnosis of Crohn’s disease.

**Complementary examinations**

First, feces exams should be performed in order to exclude infections and parasitoses. Then, the indicated exam is colonoscopy with multiple biopsies. Depending on the compromising of the mucosa, the endoscopic findings may be normal (although the biopsy can already show a certain level of histological lesion), or detect aspects such as edema, friability, granulations, and superficial or deep ulcerations, with mucopurulent mucus. In more advanced stages, colonic mobility, luminal straightening, and pseudopolyps may be visible. In the quiescent phase, the aspect of the mucosa is dry, irregular, with punctiform granulations.\(^1\)

Colonoscopy is not indicated when there is the suspicion of toxic megacolon.

The radiological exam does not provide as precise data as the colonoscopic exam, but it may be performed through a opaque edema. It may present normal in mild cases, but in moderate cases, it may show reduction of haustations, and the barium may be displayed with an aspect of ground glass. The contour of colonic walls, which is usually extremely regular, as if it were pencil-scratched, presents irregular, with spicules, ulcerations, and polypoid formations.\(^1\)

Biopsy will show either a normal mucosa or the alterations already described in the item dedicated to pathological anatomy.

Other examinations can be carried out as indicators of the disease activity (erythrocyte sedimentation and serum albumin, hemogram with leukocytosis and deviation to the right, platelet disorders), and of hepatic compromising (transaminase). The dosage of alpha-1-antitrypsin in feces is very important when bleeding is already controlled, since its values reflect the permeability situation of the mucosa, indicating quiescence or recidivism phase.\(^1\)\(^5\)

**Diagnosis**

The diagnosis is based on the clinical, endoscopic, and histological status. Initially, infections and parasitoses should be excluded, but the fact that a patient may present nonspecific ulcerative colitis in addition to an infection and/or parasitosis should be considered.

Another cause of diarrhea with sanguineous feces or with extensive mucus is the common allergic colitis in
young infants, even in those under exclusive breast-feeding. These children present diarrhea with a small volume of feces, with blood and mucus; they do not dehydrate, and present abdominal pain. The endoscopic study shows a status of lymphoid nodular hyperplasia, edema, and, eventually, little erosions, very similar to those of nonspecific ulcerative colitis. The colonic biopsy differs a little from the nonspecific ulcerative colitis, since it has less inflammatory activity, less distortion of crypts, and absence of abscesses in the crypt - although they present a great infiltrate of eosinophils. The treatment with exclusion of cow’s milk in the child’s or in the mother’s diet (in case of exclusive breast-feeding), easily resolves the case. The absence of response to this treatment requires the patient’s vigilance, as well the later reassessment in search for the confirmation of the diagnosis of nonspecific ulcerative colitis.10

**Treatment**

The therapeutic schemes depend on the severity of the case, and this graduation may be performed by different methods (Lloyd-Steel, for example), which require numerous laboratory data. The graduation proposed here is very simple, based uniquely on clinical data, and it is sufficient for the application of the therapeutic scheme with good results.

Mild form, with less than four daily evacuation, with or without blood, possibly presenting only mucus. Absence of anemia and tachycardia. These cases usually correspond to ulcerative proctosigmoiditis. The indicated treatment is the use of sulfasalazine at 70 mg/kg/day, divided in two to three doses. It is good to associate folic acid at 1 mg/day, since sulfasalazine inhibits the absorption of folic acid. The maximum dose to be given is 4 g/day. Commercialized pills contain 500 mg, but it is possible to formulate them in smaller doses, to better suit the adequate posology to infants or young children.17

Sulfasalazine is a sulfapyridine bound to 5-aminosalicylic acid by an azo ligand. It is not absorbed in the small bowel. In the colon, due to bacterial action, the azo ligand bursts, and the two fractions separate. Sulfapyridine works as a simple carrier of the 5-aminosalicylic acid fraction, which is partially absorbed by the colon, and acts on the mucosa as an anti-inflammatory, inhibiting the synthesis of prostaglandins E2, E1, and thromboxane B4.

There are other slow liberation pharmaceutical forms commercially available with only 5-aminosalicylic acid: ASACOL®, covered with acrylic polymer, which will be diluted in the colon (this does not always occur), and then 5-aminosalicylic acid is secreted; PENTASA®, covered with methylcellulose microgranules; DIPENTUM® or olsalazine, in which sulfapyridine was replaced with another radical 5-aminosalicylic acid; ASALT® or mesalazine, the only one commercialized in Brazil, also available in the form of suppository and enema (it may be used at night in mild cases, associated or not with the oral form).18

In this mild form of nonspecific ulcerative colitis, besides the drug, a diet adequate to constipation is also indicated, aiming at reducing fecal loss.

The response is favorable in few days, but the treatment should be kept for 1 month, and then reduced to the maintenance dose: one-third of the initial dose for 1 month or more, with attention to the appearance of a new episode. If the disease evolves well, the patient should be kept without drug, but the fecal dosage of alpha-1-antitrypsin in monthly intervals should be controlled, since an increase in its values is a sign of recidivism. We should remember that this mild form may extend and, with time, affect the whole colon, with more serious recidivism.

Moderate form, characterized by four to six daily evacuations, with blood, abdominal pain, discrete weight loss, discrete reduction of activities, sporadic absence at school. Treatment should be started with corticosteroid and sulfasalazine. Corticosteroids in the form of prednisone at 2 mg/kg in an only dosage are taken in the morning. With the bleeding control, a reduction in prednisone can be started, with the withdrawal of 2.5 to 5 mg of the total dose per week. Sulfasalazine will be maintained at the same initial dose, and its reduction should be carefully tried after 2 months if the clinical status is stabilized. The monthly control with the dosage of alpha-1-antitrypsin is necessary. Diet in this form should be adequate to constipation, with the reduction of cow’s milk, sugar, and leaves in the beginning; the liberation of these foods will be gradual and watched.

This is the most common form or presentation in pediatrics, and it should have long-term follow-up, with sulfasalazine maintenance dose. An acute episode frequently occurs after many asymptomatic years.

If there is no favorable response, and sanguineous diarrhea persists, retention edemas with 100 mg of hydrocortisone diluted in 100 ml of physiological serum should be associated with oral prednisone, and this scheme should be maintained for a variable time, according to the response.

Considering that nonspecific ulcerative colitis is a chronic, cyclic, recurrent disease, it can have a course of short asymptomatic phases and frequent episodes, and the patient will become either resistant or dependent on corticosteroids; therefore, there is the indication of alternative drugs, represented by immunosuppressants - the most used one, with good and safe results, is the 6-mercaptopurine, at the dose of 1.5 to 2 mg/kg/day. As the action of this drug starts late, after 2 or 3 weeks, it should be given concomitantly with corticosteroid, and the dose of the latter should be reduced only after the observation of a good therapeutic response to 6-mercaptopurine.19,20

The 6-mercaptopurine may be maintained for a long time, provided that its side effects (leukopenia and hepatic alteration) are periodically controlled.

If the patient does not respond to 6-mercaptopurine, the use of intravenous and posteriorly oral cyclosporin should be tried, but this procedure has inconstant favorable results.21
In evolutive forms, resistant to clinical treatment, with intense compromising of the general and growth status, the indication is surgery with total colectomy, definitive ileostomy, and ileorectal anastomosis.12

In refractory cases, with a more evident compromising of the distal colon, the use of retention enemas with sodium butyrate (Sigma–Aldrich®) at the concentration of 80 mmol/L in a volume of 100 ml is also indicated twice a day during 2 weeks, with an excellent result.22,23

Severe form, with more than six daily evacuations, great loss of blood, intense abdominal pain, fever, discomfort, apathy, anemia, arterial hypotension, dehydration, tachycardia. In the first or recidivous episode, the patient has to be referred to a Intensive Care Unit, and observed for the arousal of signs of toxic megacolon; in this case, he will be referred to a surgical emergency.

The specific treatment of nonspecific ulcerative colitis will consist of intravenous use of adrenocorticotropic hormone at 2 units/kg/day, or hydrocortisone at 100 mg/day or 200 mg/kg/day, rest and dietary pause, with total parenteral nutrition. If there is no satisfactory response, intravenous cyclosporin may be initiated at the dose of 10 mg/kg/day. When this severe phase is overcome, the treatment is continued with the scheme set for the moderate phase.

**Prognosis**

Since nonspecific ulcerative colitis is a recurrent disease, it presents an unforeseeable prognosis for each individual case. In a general way, its prognosis is worrying, and requires constant vigilance in the most benign cases and drug control in cases of severe evolution, becoming sometimes an incapacitating torment and provoking accentuated growth deficit.

The pediatrician, without stigmatizing the disease, will have to be alert to cases with a 10-year evolution or more, to the occurrence of colic mucosa dysplasia, and to the evolution of the disease into cancer. Colonoscopy should be performed annually.13

**Crohn’s disease**

Crohn’s disease is an inflammatory disease that affects all the digestive walls in a discontinuous way, and it may extend up to the mesentery and lymph nodes; it may be clinically manifested as a case of sanguineous diarrhea.25

**Epidemiology**

The disease is quite frequent in the North hemisphere, with an incidence of 7:100,000 people/year in the United States, and 15:100,000 people/year in Canada, according to the stabilization registration of the last decade.5,23

In Brazil, there are no official data, but it seems to have been more frequently diagnosed in gastropediatric services. It is more common in whites, does not differ in relation to sex, and it is more frequent in young adults from 20 to 40 years old; considering general population, 20% is between 10 and 20 years old, and 3% are below 10 years of age.

Studies about Crohn’s disease in the pediatric population show that 17% are below 10 years of age (the youngest case was 2 years old). In our patients, the youngest patient was 8 months of age at the beginning of the disease. As it happens in nonspecific ulcerative colitis, the delay in the diagnosis is extremely long.25

**Etiopathogenesis**

The etiology of Crohn’s disease remains unknown. The same factors discussed for nonspecific ulcerative colitis are also taken to explain Crhon’s disease etiopathogenesis:

1) The infectious factor was and still is the most studied, due to the similarity between the ileocolic form of the disease and the tuberculous ileitis; however, nothing was confirmed yet in relation to a bacterial etiology; besides, favorable response to corticoids - and not its exacerbation, as it was excepted - reinforces the improbability of this infectious theory.

2) Environmental, psychogenic, and genetic factors deserve the same considerations already done to nonspecific ulcerative colitis.5,26

3) The immunologic factor is intensely studied as a participating element in the inflammatory lesion, but also here we do not know how it starts and why it perpetuates.

A very important datum, of interest for the treatment, was the presence of a great quantity of liberation of alpha-tumoral necrosis factor in the inflamed mucosa of the patient that carries Crohn’s disease, but not in that of the patient presenting nonspecific ulcerative colitis. This cytokine has a great inflammatory potential, and is produced predominantly by the macrophages.27,28

**Pathological anatomy**

The lesion may be located at any part of the digestive tract, from the mouth to the anus, and it affects the thickness of all the wall (transmural); however, it is discontinuous, with lesion areas interspersed with normal areas. The most affected digestive segments are the ileocolic region, isolated small bowel, isolated colon, anus, esophagus, and stomach, in a decreasing order of frequency.25

The lesion is always the same, independently of its location. Macroscopically, the intestinal wall presents thickened, hardened, with reduced intestinal light, due to the intense fibrosis established. The peritoneum presents microunfoldulations similar to those found in tuberculosis; the mesentery is thickened, with lymphatic ganglions increased both in number and volume; adherence areas are also observed. The mucosa presents superficial and deep ulcerations, and sometimes fissures and fistulae. The anus may be compromised, showing fissures, fistulae and abscesses. Histologically, the mucosa presents intense lymphoplasmocytic infiltrates, neutrophils, numerous lymphoid aggregates, cryptic distortions, and in almost half
of cases, a nongasified granuloma may be identified at the lamina propria or submucosa. The presence of a great number of macrophages may be identified through immunohistochemical staining methods, using specific antimacrophage monoclonal antibodies. Through this methodology, it was also possible to show the inappropriate presence of HLA-DR expression in colonic epithelial cells in patients with Crohn’s disease, which does not occur in the normal mucosa.

**Pathophysiology**

The inflammation of the mucosa, with fibrosis, lymphatic obstruction, and edema, when located at the small bowel, may lead to malabsorption due to reduced absorptive area (epithelial malabsorption) or difficulty in transport (postepithelial malabsorption), according to Campos’ concepts. Considering the location and extension of the lesion, malabsorption may be selective or multiple. This way, if the compromised segment is the superior part of the small bowel, there will be malabsorption in relation to iron, disaccharides, proteins, folate, and fats; if the lesion is at the ileum, there will be malabsorption of bile salts and B12 vitamin.

Besides malabsorption, the organism loses protein and blood through the ulcerous lesions, and also water and electrolytes. Colonic lesion causes pathophysiologic phenomena already described in the nonspecific ulcerative colitis.

When there is the formation of stenoses, malabsorption is aggravated by the luminal mechanisms of bacterial overgrowth.

**Clinical status**

Crohn’s disease is a chronic, cyclic disease, with asymptomatic and recidivous phases. The beginning may be insidious or more abrupt, similarly to the presentation of an acute abdomen due to acute appendicitis. In this situation, the patient is operated, and eventually the surgeon does not perceive the nature of the process and dismisses the patient, which posteriorly gets worse, with symptoms or a new painful episode, feverish due to recidivism of the process at the same site; the patient may also start presenting sanguineous diarrhea as an extension to the inflammatory process at the colon. Slow beginning may present only abdominal pain, steatorrhea (if the small bowel is affected) or sanguineous diarrhea (if the colon is affected). Eventually, it may evolve with only fever, and then the patient becomes part of the group with fever of undetermined origin, of difficult diagnostic planning. Similarly to nonspecific ulcerative colitis, Crohn’s disease also presents extradigestive manifestations, and among them, articular processes; there is the possibility that Crohn’s disease is diagnosed by a careful rheumatologist, which uses abdominal X-ray or computed tomography to assess signs of inflammation in the intestine, and finds a lesion that had remained asymptomatic up to that moment.

Anyway, the symptoms will depend on the intestinal segment affected. Abdominal pain is the predominant complaint in all patients (80%); it is referred to happen in all the abdomen, or only at the right iliac fossa. The other sign that follows pain is diarrhea (70%), and it may be continuous or intermittent, little frequent but in great volume (lesion at the small bowel), or greatly frequent but with little volume (lesion at the colon), with mucus and/or blood. Tenesmus and urgency indicate lesion at the rectum and sigmoid.

Nocturnal evacuation may occur in Crohn’s disease, always indicating the compromising of the colon.

Other signs and symptoms may occur with a lower frequency, such as anorexia, nausea, vomiting, emaciation, growth deficit, and perianal disease.

Perianal disease is not very frequent in the pediatric population, but when it is present, it constitutes a serious assistance problem, and is represented by fissures, fistulae, and abscesses. It may be sometimes the first manifestation of Crohn’s disease, and we alert the pediatrician to investigate this disease when one of these lesions is found in children, even if other signs are absent.

Another rare location of Crohn’s disease that is difficult to diagnose is at the esophagus. Therefore, when there is an esophagitis that does not respond to the classical treatment for peptic esophagitis, multiple biopsies should be done, as well as the attentive analysis of histological aspects in the search for granuloma.

Extradigestive manifestations are those that compromise knee and sacroiliac articulations; in adults, the most frequent one is the ankylosing spondylitis, and all of them evolve independently of the digestive status. Dermatological lesions may also occur, such as erythema nodosum and pyoderma gangrenosum; oral lesions, such as aphthae and stomatitis; ocular lesions, such as uveitis; and digital clubbing (rare and reversible).

Crohn’s disease may be associated with hepatic diseases, such as autoimmune hepatitis, sclerosing cholangitis, and hepatic steatosis.

The physical examination of patients presenting Crohn’s disease may be practically normal or show signs of growth deficit and abdominal distention. Superficial and deep palpations may be painful; in more advanced cases, the palpation may allow the detection of masses, usually located at the iliac fossa D, where the ileum, the adjacent ganglions, and the cecum are involved in the transmural inflammatory process, and form a plastron easily identified by palpation; this semologic technique should always be performed.

The perianal region should always be examined, since there is the possibility of finding fissures, fistulae, or abscesses. Rectal touch should also be performed, in search for stenoses.

The child should be examined naked, in order to detailedly examine the skin, looking for lesions. Oral aphthae should be analyzed, as well as joint motion, in search for articular compromising.
Of the complications, the most frequent one is the formation of fistulae between the two intestinal segments, between the intestine and another organ (bladder, for example), or on skin. The other complication is stenosis (single or multiple), leading to a semiocclusive status and intensifying the general status. The installation of toxic megacolon, as well as massive hemorrhages, is less frequent than in nonspecific ulcerative colitis.

Other complications described are renal calculi, deep thrombosis, pericarditis, and pancreatitis in cases of duodenal location of Crohn’s disease.

**Complementary examinations**

First, infections and parasitoses should be excluded. If the clinical status is suggestive of steatorrhea, accompanied by intense pain, then celiac disease and mucoviscidosis should be excluded (antiendomysial antibody and sweat assay); after this, gastroenterocolonic transit should be performed.

The radiological exam through gastroenterocolonic transit may be normal or accuse the presence of lesions at the small bowel, especially at the ileum, with rigid ansae, irregular contour, thickened with ulcerations and fistulae. Stenoses with dilatations may be found. We should emphasize that these elements are not easily detected, but require follow-up with fluoroscopy and abdominal compression to individualize the ansa segments.31

The ultrasound exam may also be useful in the initial phase, but it is extremely useful when there is palpable mass, since it detects the thickening of ansae, its dilatations, and eventual liquid collections that go along with these inflammatory processes. Ultrasound also allows to follow the evolution of the process in response to the treatment.

The computed tomography also provides excellent data in moderate cases, such as about the thickening of the intestinal wall.

The colonoscopic study is essential when the diarrhea is sanguineous, and it also allows to study the ileum, through the obtainment of material to histological analysis. Colonoscopy should be also performed in cases of radiological alteration of the ileum, since this may be better assessed by colonoscopy and ileoscopy. Endoscopic findings in Crohn’s disease are hyperemia, friability, aphthoid ulcerations, and lesions (the latter are very specific of Crohn’s disease). In more serious cases, fissures, fistulae, and stenoses may be seen.25 These lesions are spread discontinuously, giving rise to aspects of lesions as caused by heels or as paved blocks, so frequently mentioned in the literature.

Biopsy will show the aspects described in the pathological anatomy. It is worthwhile to remember that the typical aspect of Crohn’s disease - the granuloma - is not always easily identified, and sometimes, the histological diagnosis has to be completed with clinical and/or endoscopic data.

Several cases of colitis do not suit nonspecific ulcerative colitis or Crohn’s disease; so, the consensus is that these cases are classified as undetermined colitis until its evolution, or until the arousal or other data make it possible to determine the diagnosis.

Other exams may be performed to study the disease activity or to assess the nutritional status, and they are the same mentioned for nonspecific ulcerative colitis.

Concerning differential diagnosis, some aspects should be considered: intestinal lymphomas, intestinal tuberculosis, deep blastomycosis, Henoch Schönlein purpura, acquired immunodeficiency syndrome, and Behcet syndrome, among others.25

**Diagnosis**

The diagnosis is clinical, and more easily performed in the presence of perianal disease or evident compromising of the ileum. In the isolated forms of small bowel, the suspicion is more difficult, and the confirmation is more complex and longer. In cases of Crohn’s disease at the colon, the differential diagnosis will be in relation to nonspecific ulcerative colitis, but by a practical and immediate point of view, this confirmation is not very important, since both diseases receive the same initial treatment, so there is time to wait for the evolution in order to define the diagnosis.

**Treatment**

The colonic form of Crohn’s disease receives the same treatment as nonspecific ulcerative colitis.

In the ileocolic form, and/or perianal disease, metronidazole is added at the dose of 15 mg/kg/day in three doses, at a maximum of 800 mg. It may be administered for several months in a continuous or intermittent way.

In cases of fistulae that do not respond to this scheme, intravenous and posteriorly oral cyclosporin is added. In cases of isolated lesion at the esophagus, stomach, or small bowel, the initial and maintenance treatment consists of corticosteroid at dosages recommended to nonspecific ulcerative colitis.

The use of 6-mercaptopurine is extremely efficient in Crohn’s disease, and it is useful as a maintenance drug for many years.19,20

Currently, in cases that are more resistant to treatment, a new drug has been being used - Infliximab (Remicade®) -, which is an antibody against the alpha-tumoral necrosis factor. Although it is very expensive, it is given in an only dose intravenously, and its effect persists for 3 months, when it is possible or not to apply another dose. This drug acts inhibiting the inflammatory biological effect of the alpha-tumoral necrosis factor, getting bound to this cytokine, which is soluble in blood, or in its transmembrane form. The use of this drug deserves more studies, but it seems quite promising.

The nutritional treatment should always be well elaborated, with a diet without residues and without lactose. Parenteral nutrition, whenever necessary, and elementary oral diets for as long as the patient tolerates them, are always useful in more severe forms.12
Many services frequently recommend diets through nocturnal probe, or even the installation of gastrostomy feeding, aiming at keeping a great nutritional status; although it is valid, this practice is difficult to carry out in our setting.

**Surgical treatment**

It is indicated in some situations, such as complications (perforation, obstruction), absence of response to clinical treatment, and serious growth compromising. The frequency of surgical indication increases with the duration of the disease.12

**Prognosis**

Crohn’s disease presents low mortality, but high morbidity, with bad quality of life. The risk for development of neoplasia is lower than that found in nonspecific ulcerative colitis.

**References**


5. Rhodes J, Thomas GAO. Smoking: Good or bad for Inflammatory Bowel Disease? Gastroenterology 1994; 106:807.


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